=> d abs fbib 1-15

L7 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN GI

$$\begin{array}{c} \begin{array}{c} R^{8}p \\ R^{7}-Ar^{1}-NH-C(Y)-NH \end{array} \begin{array}{c} E \\ V \\ Q \\ R^{9}q \end{array} \qquad I \end{array}$$

AB The present invention relates to bisarylurea derivs. (shown as I; variables defined below; e.g. 4-[4-[3-[4-chloro-5-methyl-2-(2methylaminoethoxy)phenyl]ureido]phenoxy]pyridine-2-carboxylic acid methylamide (shown as II)), their use as inhibitors of raf-kinase (no data) and for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Methods of preparation are claimed and >100 example prepns. are included. For example, 1-[2-[2-[(tert-butoxycarbonyl)(methyl)amino]ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4yl]oxy]phenyl]urea was prepared (87 %) by reacting tert-Bu [2-[2-amino-4-(trifluoromethyl)phenoxy]ethyl] (methyl) carbamate (preparation given) with p-nitrophenyl chloroformate followed by N-methyl-4-(4aminophenoxy)pyridine-2-carboxamide (preparation given) and DIPEA; deprotection gave 86 % 1-[2-[2-(methylamino)ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea. For I: Ar1, Ar2 = aromatic hydrocarbons containing 6 to 14 C atoms and ethylenic unsatd. or aromatic heterocyclic residues containing 3 to 10 C atoms and one or two heteroatoms, = N, O and S; E, G, M, Q and U = C and N atoms, with the proviso that ≥ 1 of E, G, M, Q and U are C atoms and that X is bonded to a C atom. R7 = Het, OHet, N(R11)Het, (CR5R6)kHet, et al. or R7 = -SO2-CR8:CR8-, wherein both valencies are bound vicinally to Ar1; R8, R9 and R10 = H, A, cycloalkyl comprising 3 to 7 C atoms, Hal, et al.; Y = O, S, NR21, C(R22)-NO2, C(R22)-CN and C(CN)2; g = 1-3, preferably 1 or 2, p, r = 0-5; q = 0-4, preferably 0, 1 or 2; addnl. details are given in the claims.

Ι

AN 2005:823661 CAPLUS

DN 143:229726

TI Preparation of 1,3-diarylureas as inhibitors of raf and other kinases useful against cancer and other diseases

IN Buchstaller, Hans-Peter; Burgdorf, Lars; Stieber, Frank; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank

12/19/05

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PA Merck Patent G.m.b.H., Germany
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
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FAN.	PATENT	NO.		KIN	D :	DATE		į	APPL:	ICAT:	ION 1	. 00		Dž	ATE	
PI	WO 2005	075425	5	A2	-	2005	0818	1	WO 2	005-1	EP38	7		20	0050	117
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		•	SE, SI,	•	•	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,
		MR, N	TD,	TG												

EP 2004-2092

20040130

L7 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN GI

AB Provided herein are linker compds. and conjugates that include the linker compds. In one embodiment, the linker compds. comprise 2 or 3 residues of 6-aminohexanoic acid and optionally 7-10 residues of polyethyleneglycol (PEG). The linker compds. are useful in forming conjugates with one or more components useful in biopharmaceutical or bioanal. applications. In particular, the biopharmaceutically useful compds. are kinase inhibitors. The conjugates described herein have utility in a variety of diagnostic, separation, and therapeutic applications. Thus, I was prepared from SB 202190, PEG-azide and the biotin-linker compound

Ι

AN 2005:614536 CAPLUS

DN 143:115392

12/19/05

TI Preparation of conjugated small molecules for diagnostic and therapeutic use

IN Grotzfeld, Robert M.; Milanov, Zdravko V.; Patel, Hitesh K.; Lai, Andiliy
G.; Mehta, Shamal A.; Lockhart, David J.

PA Ambit Biosciences Corp., USA

SO U.S. Pat. Appl. Publ., 63 pp.

CODEN: USXXCO

DT Patent

LA English

FAN. CNT 1

FAN.	CNT 1 PATENT NO).	KIND I	DATE	APPLICATION NO.	DATE
ΡI	US 200515	33371	A1 2	20050714		P 20040107
	WO 200506	7644	A2 2	20050728	WO 2005-US456	
		7644		20051013	2000	
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					NA, SD, SL, SZ, TZ,	· · · · · · · · · · · · · · · · · · ·
					TM, AT, BE, BG, CH,	
					IE, IS, IT, LT, LU,	
				BF, BJ,	CF, CG, CI, CM, GA,	GN, GQ, GW, ML,
	Į.	IR, NE, SN,	TD, TG			
-					US 2004-535173P	
					US 2004-557941P	P 20040330

L7 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN GI

AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

Ι

AN 2005:99470 CAPLUS

DN 142:197889

TI Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases

IN Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott

PA Bayer Pharmaceuticals Corporation, USA

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SO
     PCT Int. Appl., 68 pp.
     CODEN: PIXXD2
    Patent
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LA
     English
FAN.CNT 1
                       KIND
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                                          APPLICATION NO.
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                                           WO 2004-US23500
PΙ
     WO 2005009961
                         A2
                                20050203
                                                                  20040722
     WO 2005009961
                         A3
                                20050331
     WO 2005009961
                         B1
                                20050602
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             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
                                            US 2003-489102P
                                                                P 20030723
                                                                P 20040202
                                            US 2004-540326P
     US 2005038080
                         A1
                                20050217
                                            US 2004-895985
                                                                   20040722
                                            US 2003-489102P
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                                                                   20030723
                                                               P 20040202
                                            US 2004-540326P
L7
     ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
     The present invention provides methods for treating and/or preventing
AB
     conditions and diseases in humans and other mammals that are associated with
     and/or mediated by signal transduction pathways comprising
     platelet-derived growth factor receptor (PDGFR), especially PDGFR-\beta, by
     administering diaryl ureas. The present invention also provides devices
     and methods for treating, ameliorating, preventing, or modulating
     restenosis following angioplastic surgery or other invasive procedures
     that affect or injure the vascular system, and graft rejection following
     transplantation of a donor tissue into a host, where a stent or other
     implantable device comprises an effective amount of diaryl ureas. For
     example, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-
     methylcarbamoyl)-4-pyridyloxy]phenyl] urea, N-[4-chloro-3-
     (trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-
     fluorophenyl] urea, and N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-
     methylcarbamoyl)-4-pyridyloxy]-2-chl orophenyl]urea showed an IC50 of less
     than 10 \mu M in a pPDGFR-\beta sandwich ELISA in AoSMC cells.
AN
     2005:14200 CAPLUS
     142:86701
DN
ΤI
     Diaryl ureas for treatment of diseases mediated by PDGFR
     Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott,
IN
     William J.
     Bayer Pharmaceuticals Corporation, USA
PA
     PCT Int. Appl., 47 pp.
SO
     CODEN: PIXXD2
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     Patent
LA
     English
FAN.CNT 2
                                           APPLICATION NO.
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ΡI
     WO 2005000284
                         A2
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                                           WO 2004-US15653
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WO 2005000284

A3

20050310

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            SN, TD, TG
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                                           US 2003-520399P
                                                              P 20031117
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                                                               P 20040325
    MARPAT 142:86701
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    ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
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Diaryl ureas B-NH-CO-NH-L-(CH2)m-X-(CH2)p-L1-(Q)1-3 [I; B =
AB
       (un) substituted Ph, naphthyl, or heteroaryl; L, = (un) substituted Ph,
      naphthyl, or heteroaryl; X = bond, O, CO, NR3, NR3CO, S, CONR3, CF2, CCl2,
      CHF, CH(OH), C.tplbond.C, CH:CH, CR4R5; m, p = independently 0-4; L1 = any
      group L, 5-6 membered cyclic structure; Q = independently COR4, CO2R4,
      CONRARS; each R3-R5 = independently H, (un)substituted C1-5 alkyl, C3-5
      cycloalkyl, Ph, C1-3 alkylphenyl, C0-4 alkylheteroaryl], useful to treat
      diseases and conditions associated with signal transduction pathways
      comprising of at least one of raf, VEGFR, PDGFR, p38 and/or FLT-3. E.g.,
      a multi-step synthesis of the urea II which produced dose-dependent 45-68%
       inhibition of tumor growth in a staged HCT 116 colon (mutant k-Ras)
      xenograft model.
      2004:1154653 CAPLUS
AN
DN
       142:93545
      Preparation of diaryl ureas with kinase inhibiting activity
ΤI
      Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott,
ΙN
      William J.
      Bayer Pharmaceuticals Corporation, USA
PA
SO
      PCT Int. Appl., 122 pp.
      CODEN: PIXXD2
DT
      Patent
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      English
FAN.CNT 2
      PATENT NO.
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      WO 2004113274
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                                       US 2004-556062P
                                                           P 20040325
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OS MARPAT 142:93545

L7 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

Three-dimensional quant. structure activity relationship (3D-QSAR) AB analyses were carried out on 91 substituted ureas in order to understand their Raf-1 kinase inhibitory activities. The studies include Comparative Mol. Field Anal. (Co-MFA) and Comparative Mol. Similarity Indexes Anal. (Co-MSIA). Models with good predictive abilities were generated with the cross validated r2 (r2cv) values for Co-MFA and Co-MSIA being 0.53 and 0.44, resp. The conventional r2 values are 0.93 and 0.87 for Co-MFA and Co-MSIA, resp. In addition, a homol. model of Raf-1 was also constructed using the crystal structure of the kinase domain of B-Raf isoform with one of the most active Raf-1 inhibitors (I) inside the active site. The ATP binding pocket of Raf-1 is virtually similar to that of B-Raf. Selected ligands were docked in the active site of Raf-1. Mol. I adopts an orientation similar to that inside the B-Raf active site. The 4-pyridyl group bearing amide substituent is located in the adenosine binding pocket, and anchored to the protein through a pair of hydrogen bonds with Cys424 involving ring N-atom and amide NH group. The results of best 3D-QSAR model were compared with structure-based studies using the Raf-1 homol. model. The results of 3D-QSAR and docking studies validate each other and provided insight into the structural requirements for activity of this class of mols. as Raf-1 inhibitors. Based on these results, novel mols. with improved activity can be designed.

- AN 2004:1004044 CAPLUS
- DN 142:126552
- TI 3D-QSAR COMFA, COMSIA studies on substituted ureas as Raf-1 kinase inhibitors and its confirmation with structure-based studies
- AU Thaimattam, Ram; Daga, Pankaj; Rajjak, Shaikh Abdul; Banerjee, Rahul; Iqbal, Javed
- CS Department of Molecular Modeling and Drug Design, Discovery Research, Dr. Reddy's Laboratories Ltd., Hyderabad, 500 049, India
- SO Bioorganic & Medicinal Chemistry (2004), 12(24), 6415-6425 CODEN: BMECEP; ISSN: 0968-0896
- PB Elsevier Ltd.
- DT Journal
- LA English
- RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L7 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to

tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur) are prepared. These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 μM .

- AN 2003:874965 CAPLUS
- DN 139:364958
- TI Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors
- IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
- PA Bayer Corporation, USA
- SO U.S. Pat. Appl. Publ., 60 pp.
- CODEN: USXXCO
- DT Patent
- LA English
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
			-		
ΡI	US 2003207872	A1	20031106	US 2002-42226	20020111
				US 2002-42226	20020111

- OS MARPAT 139:364958
- L7 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- Aryl ureas of formula A-NHCONH-B [A = a substituted moiety of up to 40 AB carbon atoms of the formula: -L-(M-L1)q (where L = a 5 or 6 membered cyclic structure bound directly to D, L1 comprises a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of from 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur); B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepared These urea derivs. are useful for treating raf mediated diseases, in particular cancerous cell growth mediated by raf kinase. Thus, N-[4-bromo-3-(trifluoromethyl) phenyl] -N' - [4 - [2 - (N-methylcarbamoyl) -4 pyridyloxy]phenyl]urea. Thus, a solution of 4-bromo-3-(trifluoromethyl)phenyl isocyanate (8.0 g, 30.1 mmol) in CH2Cl2 (80 mL) was added dropwise to a solution of 4-[2-(N-methylcarbamoyl)-4pyridyloxy]aniline (7.0 g, 28.8 mmol) in CH2Cl2 (40 mL) at 0°, stirred at room temperature for 16 h, and filtered to give, after washing the yellow solids, washing with CH2Cl2 (2 + 50 mL), and drying under reduced pressure (approx. 1 mmHq) at 40° to give N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4pyridyloxy]phenyl]urea. All compds. exemplified showed IC50 between 1 nM to 10 µM against raf kinase.
- AN 2003:757329 CAPLUS
- DN 139:276918
- TI Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors
- IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott,
 William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine;
 Natero, Reina; Renick, Joel; Sibley, Robert N.
- PA Bayer Corporation, USA
- SO U.S. Pat. Appl. Publ., 61 pp.

CODEN: USXXCO

DT Patent LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	US 2003181442	A1	20030925	US 2001-993647	20011127
				US 2001-993647	20011127

OS MARPAT 139:276918

L7 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN GI

AB Aryl ureas, such as I [R = Cl, Br; R2 = OH, NH2, NHMe, NHCH2OH, alkoxy; n = 0, 1], were prepared for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R2 = NHMe, n = 1) was prepared with 57% yield by N-oxidation of I (R = Cl, R2 = NHMe, n = 0) using 3-chloroperbenzoic acid in CH2Cl2 and THF. The prepared ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

AN 2003:656745 CAPLUS

DN 139:197377

TI Preparation of aryl ureas for therapeutic use as kinase inhibitors

IN Dumas, Jacques; Scott, William J.; Chien, Du-Schieng; Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar, Ala; Riedl, Bernd

PA Bayer Corporation, USA; Bayer Pharmaceuticals Corporation

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 1

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                                       US 2002-354937P
                                                           P 20020211
                                                            A3 20030211
                                        EP 2003-707848
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OS MARPAT 139:197377

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN GI

$$\begin{array}{c|c} C1 & O & O & O \\ \hline N_{+} & O & O & M_{+} \\ \hline N_{+} & O & O & M_{+} \\ \hline \end{array}$$

The title ureas containing a pyridine, quinoline, or isoquinoline AB functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un) substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH2)mO(CH2)1, (CH2)m(CH2)1, (CH2)mCO(CH2)1, etc.; m, 1 = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

AN 2003:656581 CAPLUS

DN 139:197370

TI Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors

IN Dumas, Jacques; Scott, William J.; Riedl, Bernd

PA Bayer Corporation, USA

SO PCT Int. Appl., 67 pp. CODEN: PIXXD2

DT Patent

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English
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FAN.CNT 1
    PATENT NO.
                        KIND
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                                         APPLICATION NO.
                                                                 DATE
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                        A1 20030821 WO 2003-US4110
PΙ
     WO 2003068229
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            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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                                           US 2002-354935P P 20020211
     US 2003216396
                               20031120
                                           US 2003-361850
                         A1
                                                                  20030211
                                           US 2002-354935P
                                                               P 20020211
    MARPAT 139:197370
RE.CNT 2
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L7
     ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AΒ
     ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound
     directly to D; L1 = substituted cyclic moiety having ≥5 members, M
     = bridging group having \geq 1 atom; q = 1-3; L, L1 contain 0-4 N, O,
     S; B = (substituted) up to tricyclic aryl, heteroaryl of \leq30 C
     atoms with ≥1 6-membered cyclic structure bound directly to D
     containing 0-4 N, O, S], were prepared Thus,
4-chloro-3-(trifluoromethyl)phenyl
     isocyanate in CH2Cl2 was added dropwise to a suspension of
     4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (preparation given) in CH2Cl2 at
     0°; the resulting mixture was stirred at room temperature for 22 h. to
     afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-
     4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1
     μM. I pharmaceutical compns. are claimed.
     2003:590832 CAPLUS
AN
     139:149528
DN
TT
     Preparation of diphenylureas as RAF kinase inhibitors
     Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott,
IN
     William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine;
     Natero, Reina; Renick, Joel; Sibley, Robert N.
PA
     Bayer Corporation, USA
SO
     U.S. Pat. Appl. Publ., 62 pp., Cont. of U.S. Ser. No. 42,203.
     CODEN: USXXCO
DТ
     Patent
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    English
FAN.CNT 1
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                        KIND
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                                           APPLICATION NO.
                                                                  DATE
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PΙ
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                        A1
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A1 20020111
                                           US 2001-367380P
                                           US 2002-42203
    MARPAT 139:149528
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L7
     ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
GT
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AB Title compds. B-NHCONH-L-(M-L1)q (I) [B = (un) substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and S] and their pharmaceutically acceptable salts were prepared For example, coupling of aniline II, e.g., prepared from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 μM. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

AN 2002:850357 CAPLUS

DN 137:352907

TI Preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase for the treatment of tumors and/or cancerous cell growth

IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Robert, Sibley
N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger,
Timothy B.; Scott, William J.; Smith, Roger A.

PA Bayer Corporation, USA

SO U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 758,548. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

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	WO	2002062763			A2		2002	0815			999- 002-1					.9990 !0020		
	WO	2002	0627	63		A3		2002	1010									
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PATENT FAMILY INFORMATION:
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                           A1 20000720 WO 2000-US768
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NO	2001	0034	63		A		2001	0912		NO	200	1-3	463				20010	712

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												1999-					19990	
												1999-				В1	19991	022
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Timothy B.; Scott, William J.; Smith, Roger A.

Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, AΒ 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un) substituted 1,3- or -1,4-phenylene} were prepared Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (preparation given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compound II. Data for biol. activity of title compds. were given. AN 2002:615574 CAPLUS DN 137:169425 TI Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, IN

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AB This invention relates to the preparation and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, especially Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepared For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addition of 4-(3-N-methylcarbamoylphenoxy)aniline (preparation given) to afford the urea II.

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- DN 133:120157
- TI Preparation of ω -carboxy(hetero)aryl substituted diphenyl ureas as raf kinase inhibitors
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- PA Bayer Corporation, USA
- SO PCT Int. Appl., 120 pp. CODEN: PIXXD2
- DT Patent
- LA English
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$$\begin{array}{c|c} CT & O & O & NHMe \\ N & N & N & NHMe \\ N & N & N & N \end{array}$$

The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML1)q (wherein L = 5-6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having al least one atom; q = 1-3; each of L and L1 contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of N, O and S], useful in treating p38 mediated diseases, were prepared E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10 μ M against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

AN 2000:493376 CAPLUS

DN 133:120155

TI Preparation of ω -carboxy aryl substituted diphenyl ureas as p38 kinase inhibitors

IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PA Bayer Corporation, USA

SO PCT Int. Appl., 148 pp. CODEN: PIXXD2

DT Patent

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